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Claim 24. (Thrice Amended) An isolated peptide or polypeptide [,] consisting of an amino acid sequence from position 27 to position 229 of SEQ ID NO: 1 or 2 or a portion thereof; **wherein said peptide or polypeptide or portion thereof specifically binds to monoclonal antibody 64G12 deposited at the ECACC under no. 92022605**.

Claim 25. (Thrice Amended) An isolated peptide or polypeptide which is a fragment of the extracellular portion of the interferon receptor (IFN-R) of SEQ ID NO: 1 or 2, said peptide or polypeptide consisting of an amino acid sequence from position 1 to position 229 of SEQ ID NO: 1 OR 2 or a portion thereof; wherein said peptide or polypeptide **or a portion thereof** specifically binds to monoclonal antibody 64G12.

Claim 26. (Twice Amended) **[An analogue of]** **An isolated peptide or polypeptide which is derived from** a peptide or polypeptide as claimed in claim 23**[, which is derived from said peptide or polypeptide]** by substitution of one or more amino acid residues and which retains the ability to specifically bind to monoclonal antibody 64G12.

## REMARKS

Claims 23-26 are pending.

## I. REJECTIONS UNDER 35 U.S.C. §112, ¶1

The examiner rejects claim 26 under 35 U.S.C. §112, ¶1, allegedly because the specification does not teach one skilled in the art how to make or use the invention. Applicants respectfully traverse this rejection.

In levying this rejection, the examiner asserts that "the art indicates that substitution of a[n] amino acid(s) in parts of a protein or polypeptide molecule outside the epitope can affect the binding between the antibody and the modified protein or polypeptide." *See* Office Action mailed September 8, 2001, page 4, first full paragraph. To support this assertion, the examiner cites two articles by McGuinness *et al.*: *Lancet*, 337:514-517 (1991) and *Mol. Microbiol.*, 7:505-514 (1993).

In McGuinness *et al.* (1991), the authors taught that a point mutation generating a single amino acid change in a P1.16-specific epitope in the VR2 region of the por A gene

of Neisseria meningitidis of subtype P1.7, 16 results in "striking changes in the structural and immunological properties of the class 1 protein" of this isolate. The reference did not teach, however, that a mutation outside the epitope would result in such a dramatic change in the immunological properties of the protein.

As pointed out by the examiner, McGuinness *et al.* (1993) taught that an amino acid deletion outside an epitope is associated with loss of subtype specificity resulting from a change in the predicted conformation of the apex of the loop structure. However, this deletion comprised the removal of three amino acids (VTK), close to the epitope (ASGQ). *See* McGuinness *et al.* (1993), page 510, first column, last paragraph. As explained by McGuinness *et al.*, this deletion prevents the epitope from being accessible to the antibody in the native protein on the surface of the bacteria, whereas said protein still reacts with the P1.7-specific antibody when performing a Western blot. This shows a change in the general conformation of the whole protein, resulting in the masking of the epitope.

In addition, McGuinness *et al.* (1993) reported some "silent" amino acid changes within the VR2 epitope. *See* McGuinness *et al.* (1993), page 508, last paragraph, and page 510, first two paragraphs.

The global teachings of McGuinness *et al.* (1993) are therefore:

1. A deletion of three amino acids in a protein can change the tridimensional structure of said protein and result in the masking of an epitope.

2. A point mutation within an epitope of a protein can either lead to a change in the immunological properties of said protein, or be silent with respect to the immunological status of the protein.

Accordingly, the teachings of McGuinness *et al.* suggest that an artisan could readily identify a variant of the polypeptide having the amino acid sequence from position 27 to position 427 of SEQ ID NO. 1 or 2 or a portion thereof, wherein said variant retains the ability to specifically bind to monoclonal antibody 64G12.

Two additional arguments support this conclusion:

1. The tridimensional structure of a relatively short polypeptide of less than 400 amino acids involves fewer amino acid interactions than that of a native protein, resulting in less complex protein structures. Therefore, the probability of masking an epitope by changing the sequence outside the epitope is lower with short polypeptides, such as those of the present invention, than with native proteins.

2. One of ordinary skill in the art understands that some amino acids share similar properties with respect to hydrophobicity, polarity, charge and steric hindrance. Thus, the artisan would recognize that substitution of an amino acid in a polypeptide, especially outside an epitope, with another amino acid having similar properties is unlikely to affect the polypeptide's tridimensional conformation.

Under §112, the application must explain how to "make and use" the claimed invention. The courts have interpreted this statute to mean that the specification must teach the skilled artisan how to practice the invention without undue experimentation. *See Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 94 (Fed. Cir. 1986). Thus, the test is not whether experimentation is necessary, but whether any experimentation would be undue in view of what type and amount of experimentation is typical in the area. *See* MPEP §2164.01 (February 2000) at page 2100-130.

Applicants assert that one of ordinary skill in the art could readily make and use the inventive polypeptides without undue experimentation. Applicants submit that an artisan seeking to obtain a polypeptide different from those claimed in Claims 23-25, but having the same properties, could use the available monoclonal antibody 64G12 and the teachings of the present specification to readily obtain the claimed polypeptides. Indeed, one of ordinary skill in the art easily could produce peptides derived from those claimed in Claims 23-25 by substituting one or more amino acid residues and testing the modified peptide's ability to specifically bind monoclonal antibody 64G12. As explained above, it is probable that such mutations would not affect the immunological properties of the peptide, especially if the substitution involved two amino acids having similar hydrophobicity, charge and steric hindrance and the substitution occurred outside of an epitope.

Accordingly, Applicants assert that the experimentation necessary to find a functional variant of the peptides and polypeptides of Claims 23-25 is routine and not undue, as explained in *Ex parte Jackson*. *See Ex parte Jackson*, 217 USPQ 804 (Bd. Pat. App. 1982). Withdrawal of this rejection is therefore respectfully requested.

## II. REJECTIONS UNDER 35 U.S.C. §112, ¶2

The examiner rejects claim 26 under 35 U.S.C. §112, ¶1, for alleged indefiniteness. Applicants assert that the proposed amendment obviates the examiner's rejection.

The term "analogue" has been deleted from claim 26, which now pertains to a peptide or polypeptide derived from a peptide or polypeptide as claimed in Claim 23 by substitution of one or more amino acid residues and which retains the ability to specifically bind to monoclonal antibody 64G12. As discussed above, it is within the skill of the art to test whether a modified peptide or polypeptide of claim 23 is able to bind to the monoclonal antibody 64G12. Thus, Applicants respectfully submit that one of ordinary skill in the art readily would understand the claim terms and their scope.

## III. REJECTIONS UNDER 35 U.S.C. §102

The examiner rejects claim 24 under 35 U.S.C. §102(b) for allegedly being anticipated by Orten *et al.* Applicants assert that the proposed amendment obviates the examiner's rejection.

The examiner asserts that Orten *et al.* taught "individual amino acids that form a "portion" of the amino acid sequence from position 27 to position 229 of SEQ ID NO: 1 or 2." Office Action mailed September 8, 2001, page 5, paragraph 18. Amended claim 24 pertains to an isolated peptide or polypeptide consisting of an amino acid sequence from position 27 to position 229 of SEQ ID NO: 1 or 2 a portion thereof, wherein said peptide or polypeptide or portion thereof specifically binds to monoclonal antibody 64G12. Since individual amino acids do not constitute an epitope and can not specifically bind to monoclonal antibody 64G12, the amino acids of Orten do not anticipate the claimed invention. Accordingly, Applicants respectfully submit that in light of the proposed amendment, the rejection now is moot.

The examiner also rejects claim 24 under 35 U.S.C. §102(a) for allegedly being anticipated by Racaniello *et al.* Applicants assert that the proposed amendment obviates the examiner's rejection.

The examiner asserts that Racaniello *et al.* disclose " a "portion" of the amino acid sequence from position 27 to position 229 of SEQ ID NO: 1 or 2." *Id.* at paragraph 19. The examiner's search revealed that amino acids 1271 to 1277 of a peptide disclosed by Racaniello corresponds to the amino acids 106 to 112 of SEQ ID NO. 2.

Amended claim 24 pertains to an isolated peptide or polypeptide consisting of an amino acid sequence from position 27 to position 229 of SEQ ID NO: 1 or 2 a portion thereof, wherein said peptide or polypeptide or portion thereof specifically binds to monoclonal antibody 64G12. Since Racaniello *et al.* does not contain any information

about the reactivity of the amino acid sequence disclosed by Racaniello with the monoclonal antibody 64G12, the disclosure can not anticipate the present invention. Accordingly, Applicants respectfully submit that in light of the proposed amendment, the rejection now is moot.

## IV. OBJECTIONS

The examiner objects to claims 23 and 25 for lacking a second recitation of the term "a portion thereof." Applicants assert that the proposed amendment obviates the examiner's rejection.

In view of the foregoing amendments and remarks it is believed that the application now is in condition for allowance. A favorable disposition of the application therefore is solicited. The examiner also is invited to contact the undersigned if there are any questions or if the examiner believes that further discussion will advance prosecution.

Respectfully submitted,

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Date

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